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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,222	06/05/2006	Michael Soeberdt	041165-9092-00	7828

23409 7590 03/03/2008

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EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
03/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,222	SOEBERDT ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/20/05 & 4/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1,5-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Nature of ring members for NR7R8 rings is not completely set forth in main claim 1 and specification provides no guidance as to what type of rings are suitable except for mention of those in dependent claims 2-4. Note In re Wiggins 179 USPQ 421 regarding such terminology.

2. Claim 6 is of indeterminate scope . Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood. Additionally, determining whether a given disease responds or not to “modulation” of the MC-4 receptor involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Thus what “success rate” determines if a particular drug is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two is whether applicants have clearly defined “their” invention not what

may be discovered by future research as this type of claim language clearly requires.

3. Intended scope of claim 5 is not clear. "Medicament" is recited which implies additional components. If such are intended then the claim is a substantial duplicate of claim 15. Specification does not teach administration of instant compounds neat as far as the examiner can determine.

4. Nature of substituents for alkyl/cycloalkyl groups in R7/R8 is never described in the specification as far as the examiner can determine.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for free base and salt forms, does not reasonably provide enablement for scope of solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and thus use the invention commensurate in scope with these claims. Solvates are nonenabled since generally not all solvents can form solvates with all compounds. There is no process enabling such a scope in the specification . Note Vippagunta provided in herein who flatly states on p.18, section 3.4 the following: "Predicting the formation of solvates or hydrates of a

compound…. Is complex and difficult." Applicants' own specification confirms this since despite numerous examples presented none of the final products were obtained as solvates.

Claims 1 and 5-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Scope of piperazine/piperidine/azepine/diazepine compounds embraced within formula (I) is not adequately enabled. While many compounds have been described only a few have been tested and these are consistently of a similar substitution having Ar as aryl with R2 being chromone and with **monocyclic** moieties corresponding to the R3 scope embraced in claims 2-4. It is noted that the R2 ring system can be further fused but starting material sources to support such a scope is not seen in the specification . Note In re Howarth 210 USPQ 689; Ex parte Moersch 104 USPQ 122. From a reading of the specification the scope of heteroaryl/heterocyclic rings include not only monocyclics but also fused systems both saturated, partially unsaturated and heteroaromatics The only compounds having

this type of substitution have a triazolyl, or imidazolyl ring at instant R3. However, there is no reasonable assurance as to what other substituents will work as there is no test data **representative** of the instant scope and thus no structure-activity trends that can be evaluated. Receptor binding is known to be structure-sensitive in general. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition which considers such factors as:

1) Breadth of the claims- the scope easily totals in the millions if not billions;

2) Level of unpredictability in the art – the invention is pharmaceutical in nature involving binding activity at a particular receptor (melanocortin-4). It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18;

3) Direction or guidance- as stated above substituted compounds actually made and tested are representative of the scope in dependent claims but not remaining scope;

4) State of the prior art- while there are piperazines/diazepines of similar backbone that are asserted for possessing the activities described herein the art does not also not support such a scope by way of testing commensurate with the instant scope;

5) Working examples- Only assay test data has been presented for 11 compounds and thus no clear evaluation of which hetero rings at various positions coupled with varying central ring and ring system at R2 out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

Claims 6-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The method claims for treating **as well as preventing** various uses are not enabled based solely on specification's description that instant compounds have

activity as melanocortin-4 receptor antagonists or agonists. No clear evaluation of their relevance to *in vivo* efficacy for any one use is ever set forth and no actual test data in recognized animal model(s) has been reported. See In re Stevens 16 USPQ 2d 1379 regarding sole reliance on description of testing protocol.

Note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition, which includes factors such as:

1) Breadth of the claims- The claims cover compounds easily in the millions;

2) Level of unpredictability in the art- The invention is pharmaceutical in nature involving activity at a particular receptor type (MCH). It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be unpredictable. See In re Fisher 166 USPQ 18. The Sebhat publication cited herewith which is contemporaneous with applicants' priority date emphasizes the preliminary stages of research in this area. While obesity has been strongly linked to this receptor, it is MC-4 agonists that have been correlated to treating this disorder yet most of

applicants' compoundsthat have been tested are antagonists. MC-4 antagonists appears to be less studied as indicated on p.36 of the article;

3) Direction or guidance- The amount of guidance presented in the specification as to which compounds are sufficiently active to be useful for the claimed uses is nonexistent. The dosage range information (on p.16) is virtually useless being a 100,000 fold range and not directed to a specific disease;

4) State of the prior art- Obesity is the most strongly linked use in the MC-4 art as can be seen from the reference provided;

5) Working examples- Only assay test data has been presented for a limited scope. By far most of the compounds are antagonists. It is stated that compounds can be antagonists or agonists but its not clear for what uses antagonists are known . Note again, the Sebhat article in which the focus is more on agonists. Thus in the absence of animal studies and in the absence of any correlation between studies conducted **in vitro** and the diseases to be treated, there is no sufficient evidence to support the claimed uses.

In view of the above considerations, this rejection is being applied.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute)

so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/549942. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter claimed herein is also embraced by the claims in the copending case. While the claims are very generic, specification on p.22 describes as preferred the sidechain moiety on phenyl ring always required herein, namely pyrrolidinones and homologs thereof. While species in the

copending case have isoquinoline in place of instant R2, the ring systems recited herein are also claimed in the copending case as alternate choices.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Bernhardt/
Primary Examiner, Art Unit 1624